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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,788	01/06/2000	THOMAS JOHN BALDWIN	5673-53922	1383

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,788	BALDWIN ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-44* is/are pending in the application.

4a) Of the above claim(s) *28-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *25-27 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/03,8/03,10120/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 25-27 and 45 in the paper filed December 2003 is acknowledged. The traversal is on the ground(s) that it would not place an undue burden on the Examiner to search both Groups I and II together because both Groups comprise a bacteria with a mutated *fur* gene. This has been carefully considered but is not found persuasive because the special technical feature of Group I is a vaccine comprising a non-viable preparation comprising bacterial membrane antigens from cultured cells of a mutant bacterium having a genome wherein the *fur* gene has been modified by mutation so that expression of its gene product is regulated independently of the iron concentration in the environment of the bacterium. This is a different product than is recited in Group II which is an attenuated bacterium. This special technical feature is structurally and biologically different from that of Group 1 because the special technical feature of Group 1 is non-viable and made up of antigens whereas the special technical feature of Group II is an attenuated (live) whole cell. The search for a vaccine comprising bacterial membrane antigens and one containing a live attenuated bacterium would not be coextensive.

The requirement is still deemed proper and is therefore made FINAL. Claims 28-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Sequence Compliance

2. It is noted that Figure 2 of the instant specification recites a nucleotide/amino acid sequence which is encompassed by the definitions for nucleotide sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The M.P.E.P., Section 2422.02, 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide/amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide sequences that fall within the definitions. When a sequence is presented in a drawing, regardless of the format or the manner of the presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings. It does not appear that the sequence recited in Fig. 2 is in the Sequence Listing. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Additionally, the instant specification also contains several nucleotide/amino acid sequences throughout the specification which are also encompassed by the definitions for nucleotide/amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) and which must conform with the sequence rules for all applications that include

nucleotide/amino acid sequences. The sequence identifiers obtained through conformance (paper submission and CRF/electronic) must be inserted into the body of the specification directly following the sequence. Pages 23-25 were found to contain sequences which meet the definition for compliance. Additionally, Applicants are responsible for meeting compliance with any sequence the Examiner may have inadvertently missed. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Specification

The disclosure is objected to because of the following informalities: in the 'Brief Description of Drawings' on page 6. 'Figure 3' should be changed to 'Figure 3(i)-3(iv)' and 'Figure 5' should be changed to 'Figure 5A-5D'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 and 45 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is vague and indefinite because it is unclear whether the claimed vaccine composition can contain both (a) (i) and (a) (ii) or if it can only contain one or the other. Additionally the claim recites "antigenic material selected from:" and it is unclear if this means that the antigenic material is isolated from the attenuated live mutant of (a)(i) or is the mutant itself.

Claim 25 is also vague and indefinite because it is unclear what is meant by 'regulated independently of the iron concentration in the environment' because it is unclear whether this means that the fur protein can be produced whether iron is present or not present. Does this mean that the fur gene is expressed even when iron concentrations are high? If so, then it should be stated this way in the claim. Additionally, it is unclear how the gene is 'modified' to achieve this yet still allow for the bacterium to retain immunoprotective abilities. The claim fails to provide the structure responsible for the function.

Claim 25 is vague and indefinite because it does not describe what modification has been made to the *fur* gene in order to accomplish the claimed function. The claim attempts to claim a product through functional limitations alone. However, the mutation is critical to the invention. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the

claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Applicants should provide the location of the mutation in order to allow for one to understand the metes and bounds of the invention. Are deletions being made to the fur gene?

Claim 45 is vague and indefinite because it recites a 'method of treating a subject which is a human or non-human animal' by vaccinating a subject using the vaccine of claim 25, yet the claim fails to teach what the subject is being treated for. The claim is vague and indefinite because it is unclear what disease, infection or ailment vaccine is being treated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-27 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are broadly drawn to a vaccine composition which comprises antigenic material selected from: (i) ***any*** attenuated live mutant bacterium having a genome wherein a native gene having a function of ferric uptake regulation (fur gene) has been modified by mutation whereby expression of a gene product corresponding to

said fur gene is regulated independently of the iron concentration in the environment of the bacterium; and (ii) a non-viable preparation comprising bacterial membrane antigens from cultured cells of a mutant bacterium ***(of any Genus/species)*** having a genome wherein a native gene having a function of ferric uptake regulation (fur gene) has been modified by mutation whereby expression of a gene product corresponding to said fur gene is regulated independently of the iron concentration in the environment of the bacterium; together with a pharmaceutically acceptable diluent or carrier. Methods of using said vaccine to treat a human or non-human animal through the administration of said vaccine are also claimed. However, the claims fails to recite what the animal is being treated for.

The instant specification fails to provide any results from experiments in which either the attenuated live bacterium or membrane antigens from said bacterium were used to treat an animal for any condition. Further, page 4, lines 10-16, of the instant specification state that 'the present invention is based on the finding that altering the regulation of the ferric uptake regulation (*fur*) gene in *N.meningitidis*, such that expression is independent of the iron concentration in the environment of the bacterium, enhances the expression of important protective antigens when the bacterium is grown in culture." The specification goes on to state that this has important implications because this should increase the efficacy of said live vaccine. However, it is noted that the scope of the instant claims is not limited to *N.meningitidis*, but includes any bacterium, even those which differ greatly from *N.meningitidis,* provided they possess a gene involved in ferric uptake regulation. The prior art teaches that the menigococcal

fur gene is the most divergent of bacterium which possess it and that it appears to be essential in the N.meningitidis species. See Thomas et al (Mol.Microb. 1994.11(4):725-737. It is noted that the instant specification provides only broad prophetic examples of how to mutate the fur gene in order to obtain the desired result. Further, no results are shown to demonstrate that any of these prophetic constructs will have success as a vaccine. Even more notably lacking, is any examples of using non-viable membrane antigens from these mutant bacterium and their success as vaccines. Additionally, it does not appear that bacterial membrane antigens obtained from the cells of the mutant bacteria will differ from cells of wild-type bacteria. The same antigens will be present so it appears that they would be the same preparations. There are no results which demonstrate these non-viable preparations success as vaccines. The bacterial vaccine art is highly unpredictable. A good immune response is not directly correlated to a *protective* immune response. The only teaching of the use of membrane vesicles is at page 19, lines 15-20, where it is stated that 'in addition to the live attenuated vaccine, membrane vesicles derived from the mutated, attenuated N.meningitidis or other vesicle-producing bacteria may be a better option for certain patients or patient groups. N.meningitidis and other bacteria naturally produce membrane vesicles which may be isolated. These may be used directly to induce a strong immune response." However, no working examples or guidance is provided. This is insufficient to enable the invention since the bacterial vaccine art is so unpredictable.

Additionally, it is unclear how the *fur* gene can be modified so that it is regulated independent of the iron concentration in the environment and so that the bacterium will

possess immunoprotective abilities. It is unclear that all of the different modifications which are possible to allow for the *fur* gene to be regulated independent of the iron concentration in the environment would provide an attenuated bacterium which would be successful as a vaccine. No results are provided with the various mutants recited in the specifications and their effectiveness as vaccines. Further, the specification only provides a discussion of possible modifications to be made and they are directed to solely *N.meningitidis*. These are only prophetic examples. No results are shown to demonstrate that any of these prophetic constructs will have success as a vaccine. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." That requirement has not been met in this specification. The specification is non-enabling, since one skilled in the art would not be able to make and use those sequences without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-27 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Allan et al (WO 94/05326).

Allan et al teach bacterial vaccines to protect against pathogenic bacteria. Allan et al teach the use of live, attenuated mutant bacteria. Allan et al specifically teach that mutations can be made in the *fur* gene. See page 12, lines 1-29. It is taught that mutants having a fur mutation which causes reduced synthesis of a protein involved in regulation of iron intake is preferred. Mutants defective in iron metabolism are also taught. These mutants would inherently have a fur gene which is 'regulated independently of the iron concentration in the environment'.

12. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

J Graser 3/4/03

Jennifer Graser
Primary Examiner
Art Unit 1645